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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,111	INPANBUTR, NONGNUCH	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-12,18-26,28-37,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12,18-26,28-37,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed May 6, 2004 have been entered.

Claims 1-6, 8-12, 18-26, 28-37, and 39-40 are pending.

The outstanding objection is withdrawn in view of the amendments filed May 6, 2004.

The outstanding rejections under 35 USC 112, first and second paragraph are withdrawn in view of the amendments filed May 6, 2004.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 8-12 and 23-26, 28-37, and 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boggolini et al. (USPN 5,087,619) and Abdaimi et al.

(Cancer Research, 1999; 59:3325-3328), insofar as it relates to the *in vivo* method of treating squamous carcinoma.

Boggiolini et al. teaches a method of treating neoplastic diseases in a warm-blooded animal comprising administering an effective amount of a vitamin D3 analogue (e.g., 1,25 (OH)2 D3 and 1,2-16 delta-23-yne-D3) (see for example tables III and IV, claim 20 and abstract). Boggiolini et al. also teaches the vitamin D compounds therein are useful in effectively against human squamous carcinoma cell lines (See col. 15, line 32-48, Table III). Boggiolini et al. also teaches vitamin D3 analogues in oral dosage forms such as capsules, see col. 21, lines 37-40. Pharmaceutically acceptable carrier materials may be incorporated in capsules, such as starch, magnesium stearate, lactose, peppermint oil (flavoring agent) (see in particular col. 21, line 37 to col. 22, line 27). Boggiolini et al. also teaches that the dosage for the vitamin D3 analogues is 0.1 to 10 microgram per day (see col. 11, lines 16-24).

Abdaimi et al. teaches that EB1089 is known to inhibit cell proliferation and is useful against squamous carcinoma (See page 3327, col. 2, third paragraph).

Boggolini et al. and Abdaimi et al. taken together do not teach the doses claimed herein in terms of nmol/Kg, neither do they teach all the pharmaceutical excipients and auxillaries claimed herein. Boggolini et al. and Abdaimi et al. also do not teach the method of treating SCC 2/88 cell lines. Boggolini et al. and Abdaimi et al. taken together do not teach the administration of the active through feed the dog with pet food with the herein claimed materials.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ/express the amounts of active in terms of nmol/Kg. It would have also been obvious to employ any known pharmaceutical excipients and auxillaries in the composition employed in the instant method. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the herein recited vitamin D compounds to treat squamous cell carcinoma. It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the active through feeding the active to the animal along with food substance.

One of ordinary skill in the art would have been motivated to employ/express the amounts of active in terms of nmol/Kg because optimization of amounts is within the skill of the artisan and is therefore obvious. Similarly the employment of any known pharmaceutical excipient and/or auxillaries with a known active is within the skill of the artisan and therefore obvious. Furthermore, providing the pet with medication through feed is considered a routine practice for providing medication to animals. Therefore, absent any evidence to the contrary, such method step is rendered obvious by the cited prior arts.

One of ordinary skill in the art would have been motivated to employ the herein recited vitamin D compounds to treat squamous cell carcinoma. The preferred vitamin D compounds herein are known to be useful in treating human squamous carcinoma. Employing the same compounds for treating a canine squamous carcinoma would be reasonably expected to be successful since the compounds herein are known to be

useful in any warm-blooded animal for fighting against squamous carcinoma, absent evidence to the contrary (See Boggolini et al.).

Claims 6 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boggolini et al. and Abdaimi et al. as applied to claims 1-5 and 7-12 and in further view of Katzung (Basic and Clinical Pharmacology, p.661-663, 838, 841, 830-832 and 537-538) and Hardman et al. (Goodman and Gilman's The Pharmacological Basis of Therapeutics, p.539), all of record in the previous office action.

Boggiolini et al. and Abdaimi et al. suggest the method of treating canine squamous carcinoma by employing the herein claimed vitamin D compounds.

Boggiolini et al. and Abdaimi et al. taken together do not teach the inclusion of a second active (i.e., bone agent, cytotoxic agent or anti inflammatory agent) in a composition employed in a method of treating cancer. Boggolini et al. and Abdaimi et al. taken together do not teach the administration of the active through feed the dog with pet food with the herein claimed materials.

Katzung teaches that hypercalcemia is a consequence of hypervitaminosis D. Katzung further teaches that bisphosphonates, calcitonin are employed in treating hypercalcemia, see pages 661-663. Katzung also teaches the employment of estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil for treating different cancers, see page 838 and 841. Katzung further teaches cisplatin, melphalan, and methoxorate as anti-cancer agents, see pages 830-832. Both Salicylates and Naproxen are known NSAIDS (known for their anti-inflammatory and analgesic properties), 537-538.

Hardman et al. teaches that pain is commonly associated with cancer, see page 539.

It would have been obvious to one of ordinary skill at the time the invention at the time the invention was made to employ a second active (i.e., bone agent, cytotoxic agent or anti inflammatory agent) in a composition employed in a method of treating cancer. It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the active through feeding the active to the animal along with food substance.

One of ordinary skill in the art would have been motivated to employ bisphosphonates and calcitonin in a method of treating cancer employing a vitamin D3 analogue/derivative because they are known to be employed in methods of preventing and/or treating hypercalcemia associated with vitamin D administration. One of ordinary skill in the art would have been motivated to employ Salicylates and Naproxen, known NSAIDS, known for their anti-inflammatory and analgesic properties, in a method of treating cancer because pain is known to be associated with cancer. Furthermore, providing the pet with medication through feed is considered a routine practice for providing medication to animals. Therefore, absent any evidence to the contrary, such method step is rendered obvious by the cited prior arts.

One of ordinary skill in the art would have been motivated to employ estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil cisplatin, melphalan, and methoxorate along with Vitamin D derivatives in a method of treating cancer. Estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil cisplatin, melphalan, and

methoxorate are known to be employed in methods of treating cancer. Combining two agents which are known to be useful to treat cancer individually into a single composition useful for the very same purpose (i.e. treating cancer) is prima facie obvious (See *In re Kerkhoven* 205 USPQ 1069).

Response to Arguments

Applicant's rebuttal arguments in pages 7-9 averring the cited prior art's failure to teach the method step of providing the pet food with medication have been considered, but are not found persuasive. Providing the pet with medication through feed is considered a routine practice for providing medication to animals. Therefore, absent any evidence to the contrary, such method step is rendered obvious by the cited prior arts.

Applicant's rebuttal arguments averring the cited prior art's failure to provide motivation to combine the teachings of the prior art have been considered. The motivation to combine is based on the fact that the herein claimed agents are useful in treating cancer. It flows logically to concomitantly employ both agents, which are known to be useful for treating cancer, for the method of treating the very same disease, absent evidence to the contrary.

Applicant's arguments filed May 6, 2004 averring the individual cited references not teaching the instant invention have been fully considered but they are not persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413,

208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, when taken the cited prior art together as a whole, one of ordinary skill in the art would have been reasonably expected to employ the herein claimed compounds to a method of treating a squamous cell carcinoma cell line.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Patent Examiner
Art Unit 1617